

Galanin Expressing Leptin Receptor Neurons and Their Role in Anorexigenic Leptin Action

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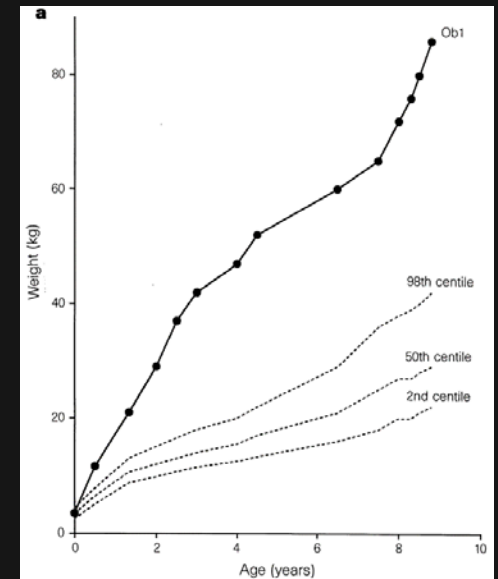
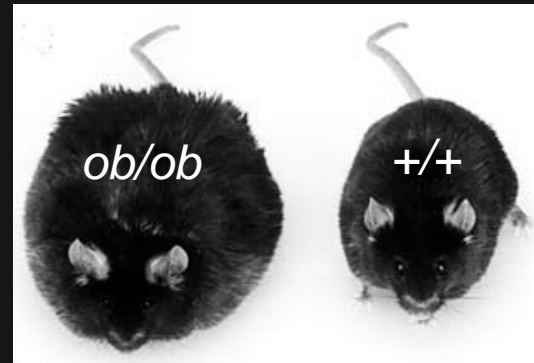
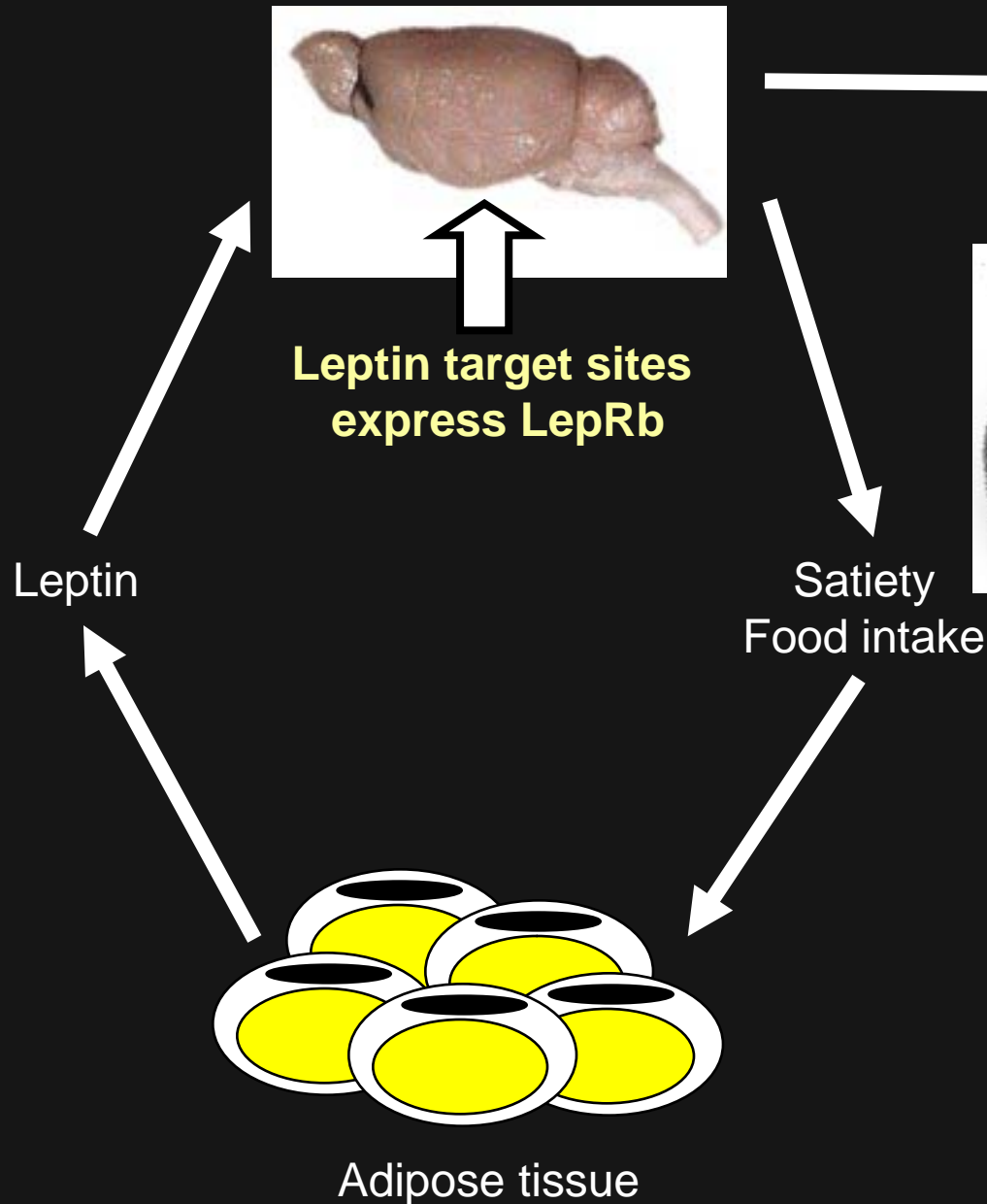
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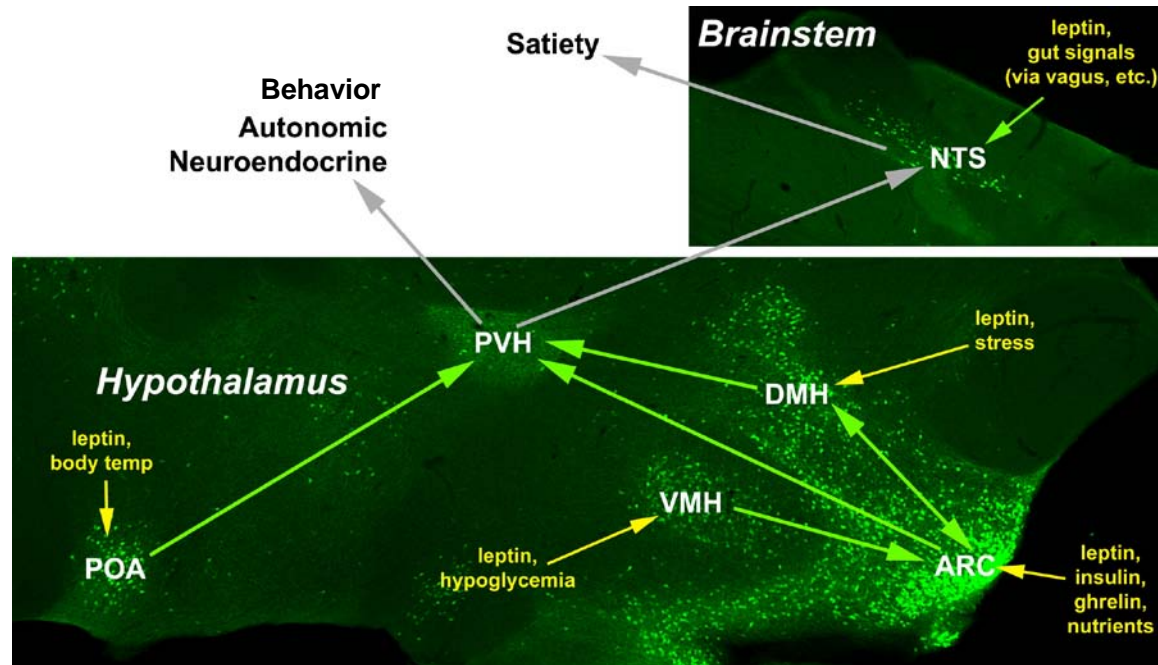
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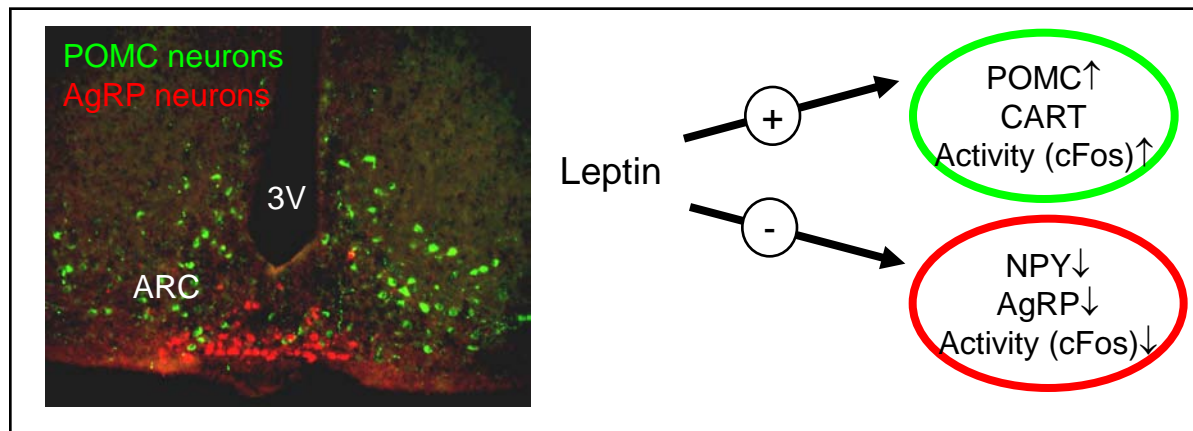
Leptin



LepRb expression in the CNS

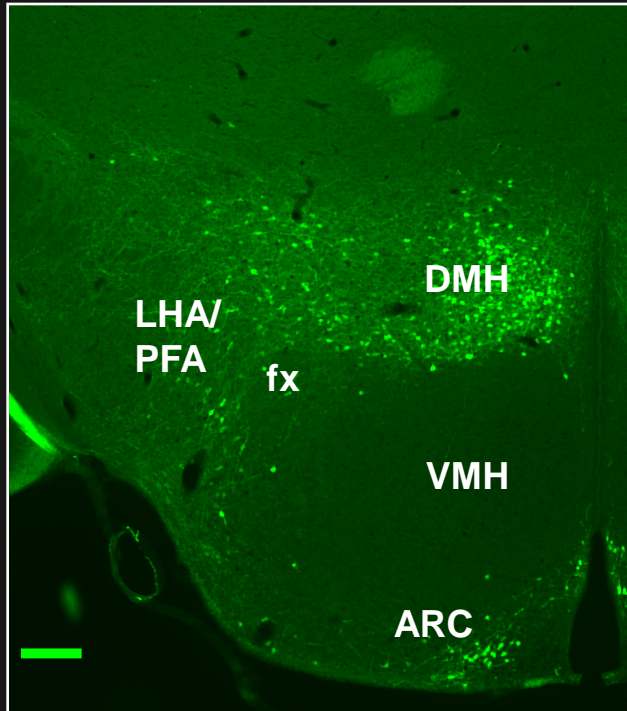


Myers MG, Jr, Munzberg H, Leininger GM, Leshan RL, *Cell Metab* 9:117-123, 2009



Galanin

Galanin^{TgGFP} mouse, IHC: GFP

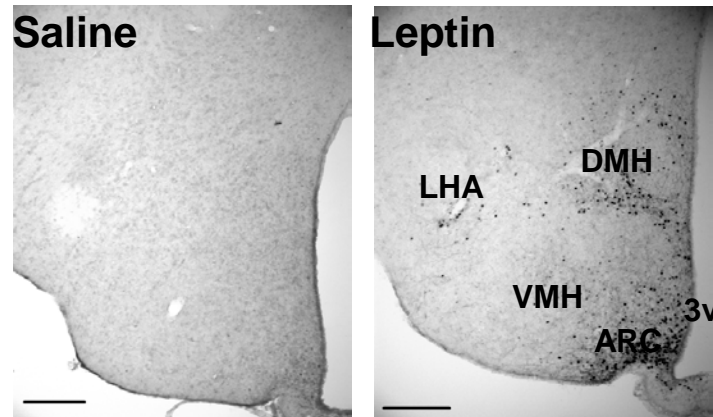


Orexigenic neuropeptide (29 AA)
specific induction of fat intake

Orexigenic action proposed to be mainly mediated
via action in the PVN

Literature on interaction of leptin and galanin
system very controversial with regard to
LepRb/galanin co-localization.

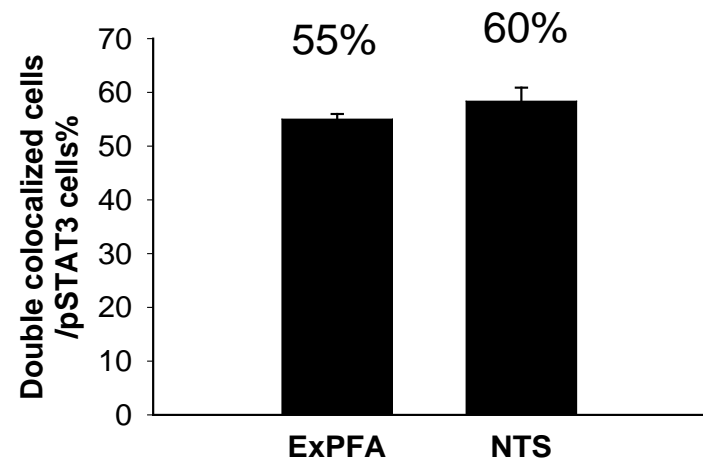
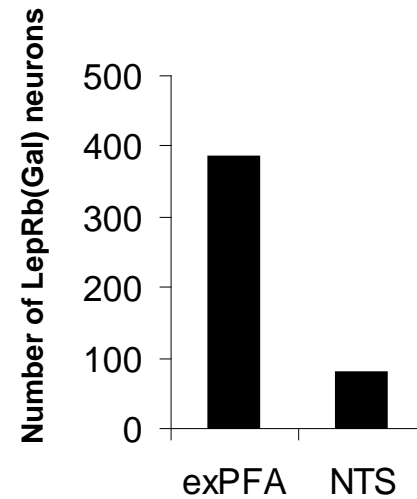
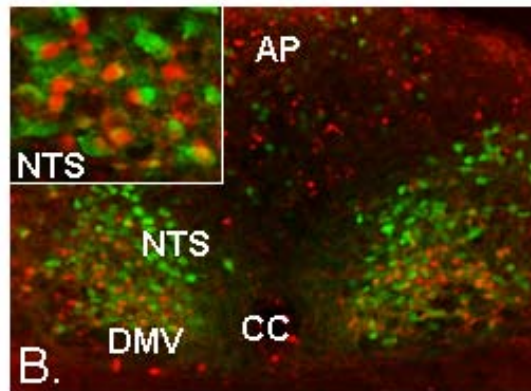
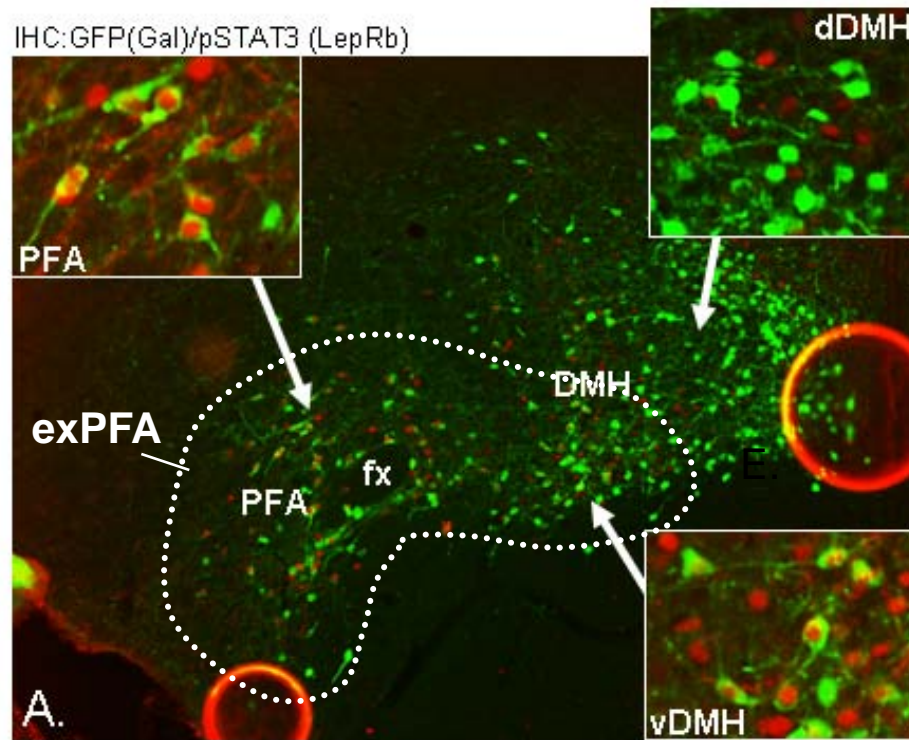
Leptin induced pSTAT3 as a marker for LepRb



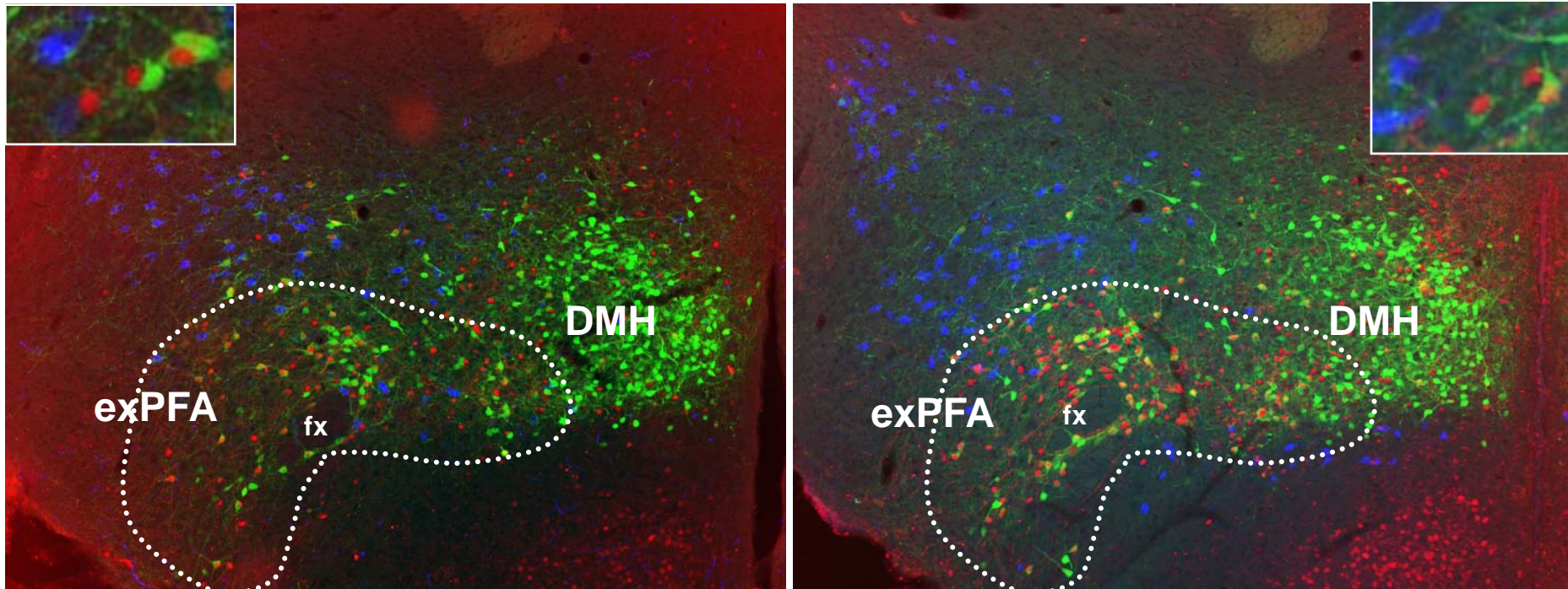
Fasted wt mice
30' treatment

IHC: P-STAT3

LepRb Neurons in exPFA and NTS Co-Express the neuropeptide Galanin



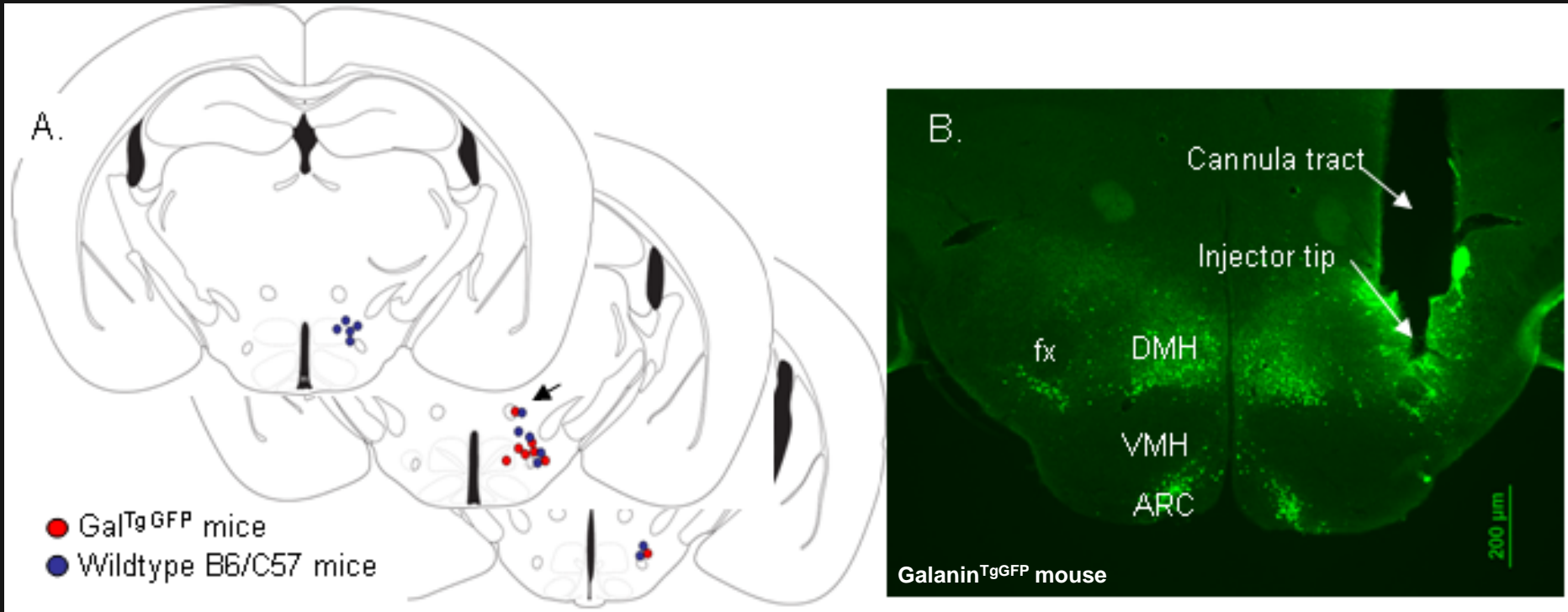
LepRb(Gal) Neurons are Distinct from Other Orexigenic Neurons Known in the Perifornical Area



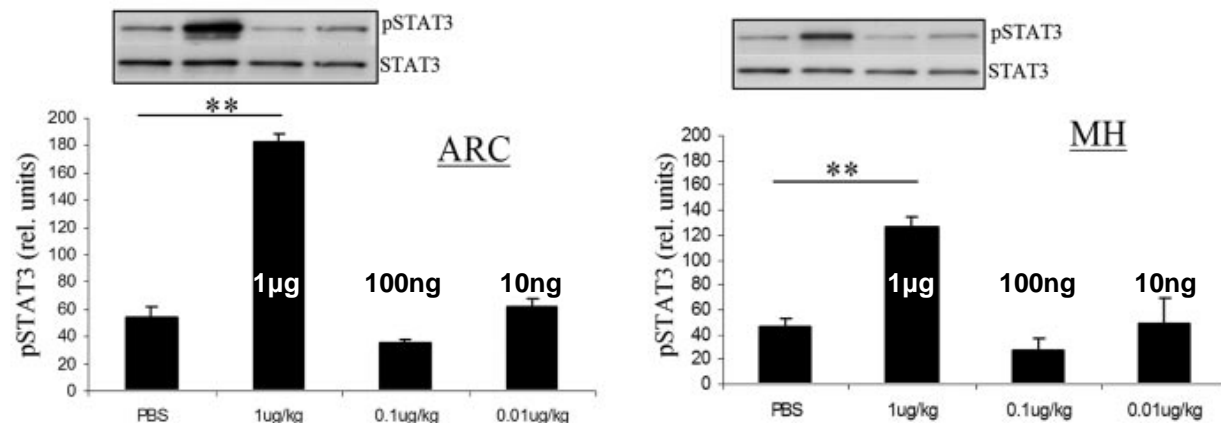
orexin
GFP (Gal) (green)
pSTAT3 (LepRb) (red)

MCH
GFP (Gal) (green)
pSTAT3 (LepRb) (red)

Unilateral cannulation of the exPFA to measure anorexigenic leptin effects



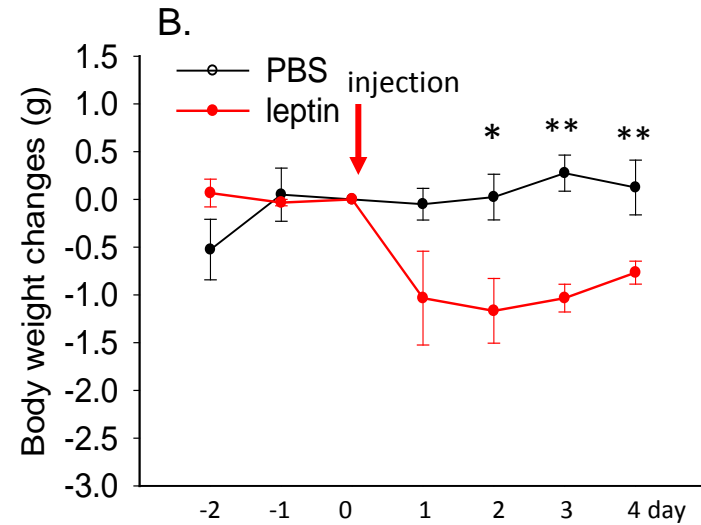
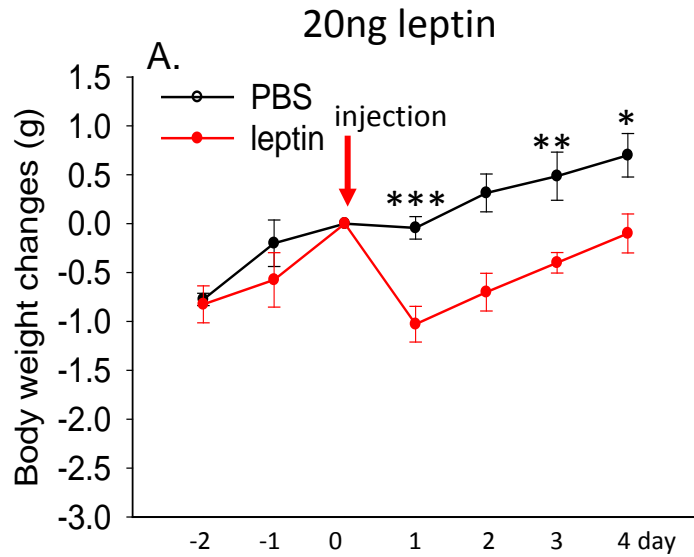
C IB: P-STAT3/STAT3, dose response i.c.v. leptin (30min)



Leptin Action in the exPFA Regulates Body Weight and Food Intake

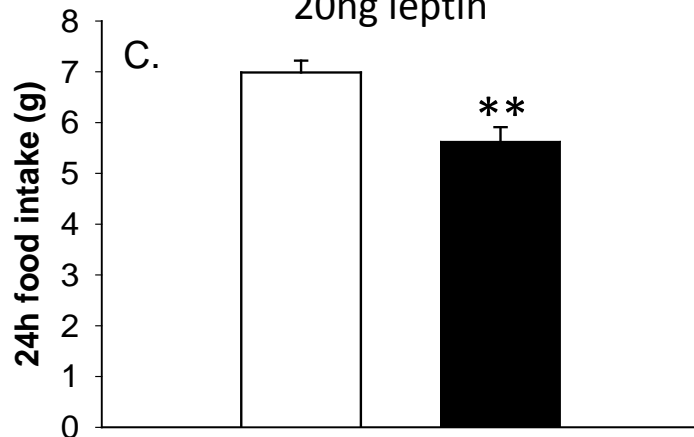
Leptin injection into the exPFA reduces body weight

1ng leptin

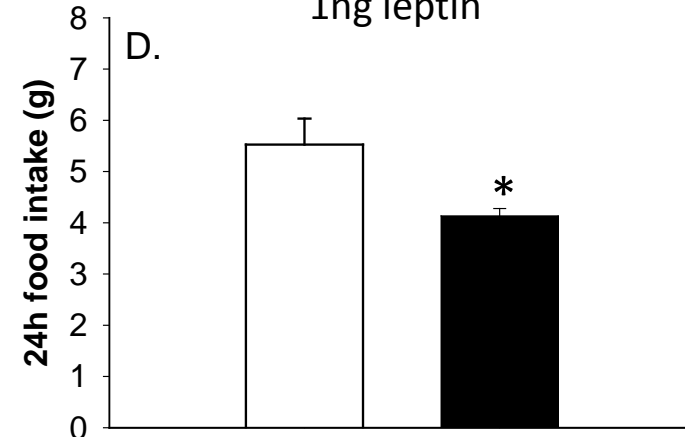


Leptin injection into the exPFA reduces food intake

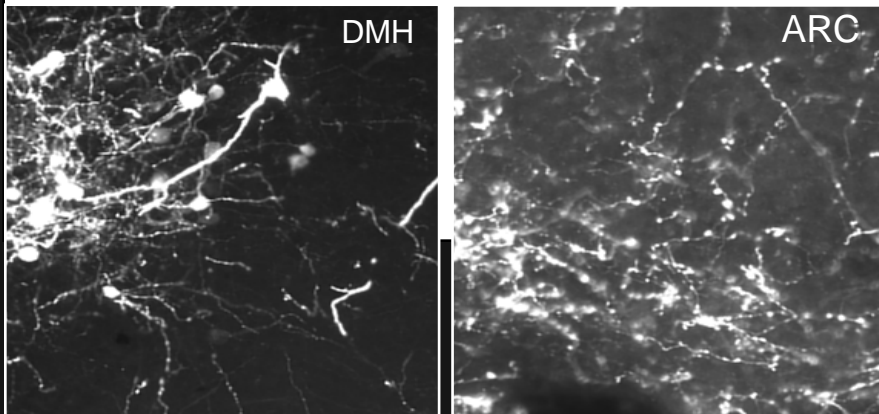
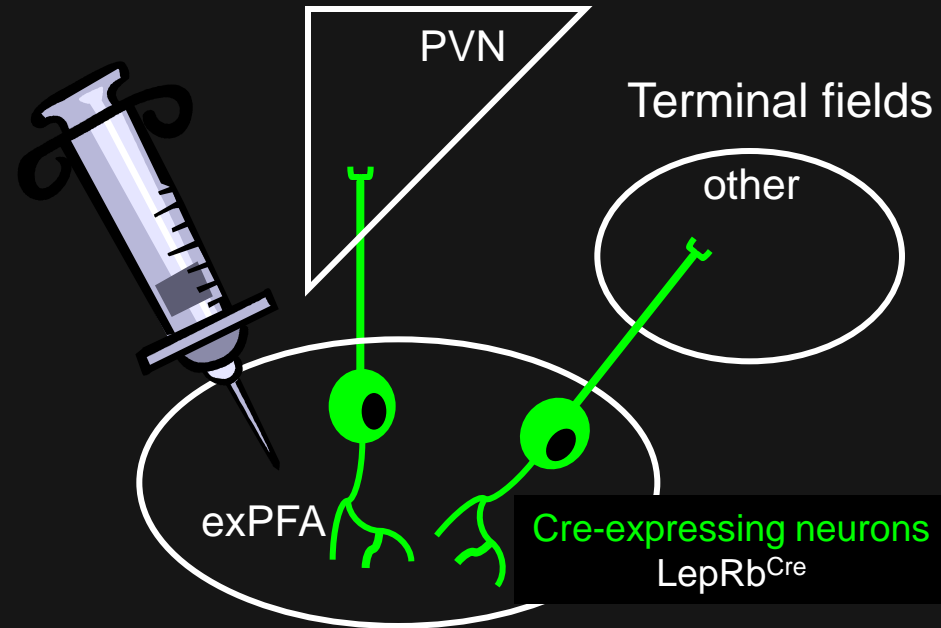
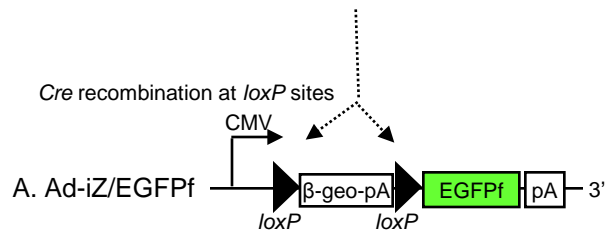
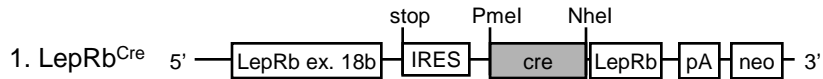
20ng leptin



1ng leptin



- Conditional Tracing: Viral cre/loxP System – Do exPFA LepRb Neurons innervate the PVN?



LepRb specific:

EGFPf expression only in cre-expressing neurons

Site specific (e.g. exPFA):

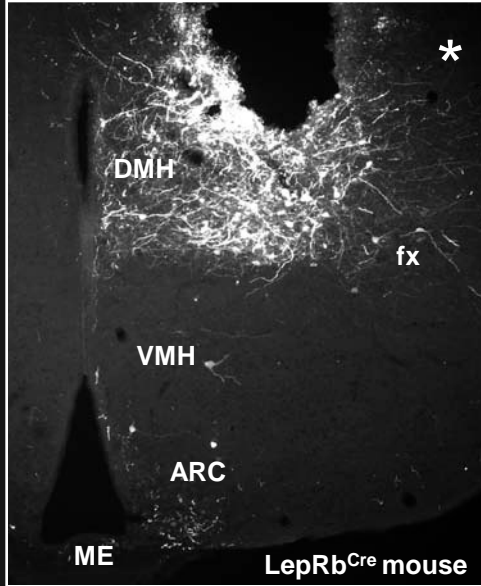
stereotaxic injections

Visible dendrites and axons:

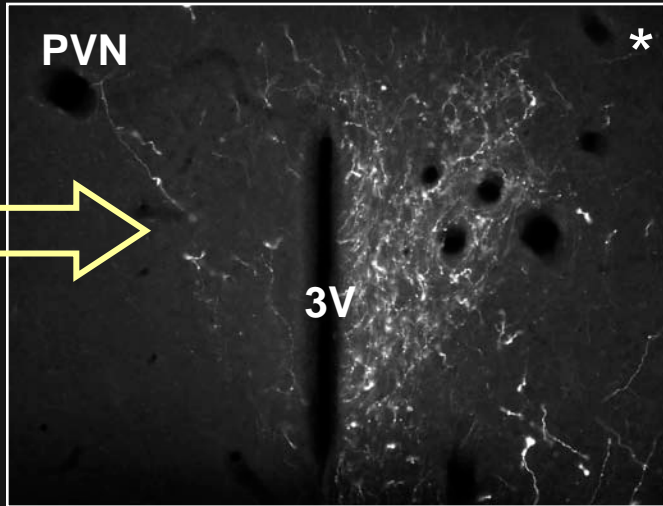
Farnesylated EGFP

LepRb Neurons in the exPFA project to the PVN

vDMH LepRb neurons

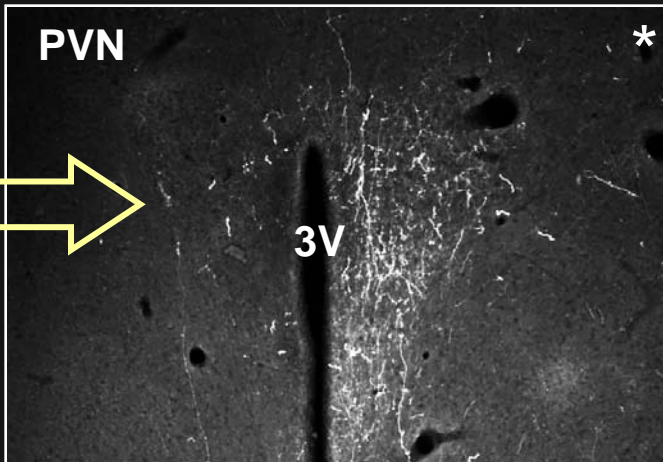
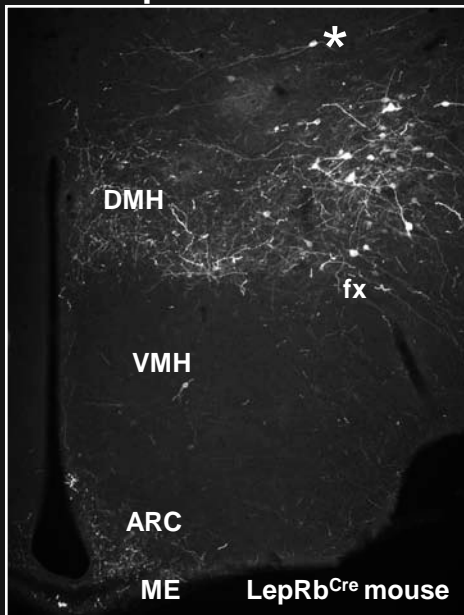


IHC: GFP

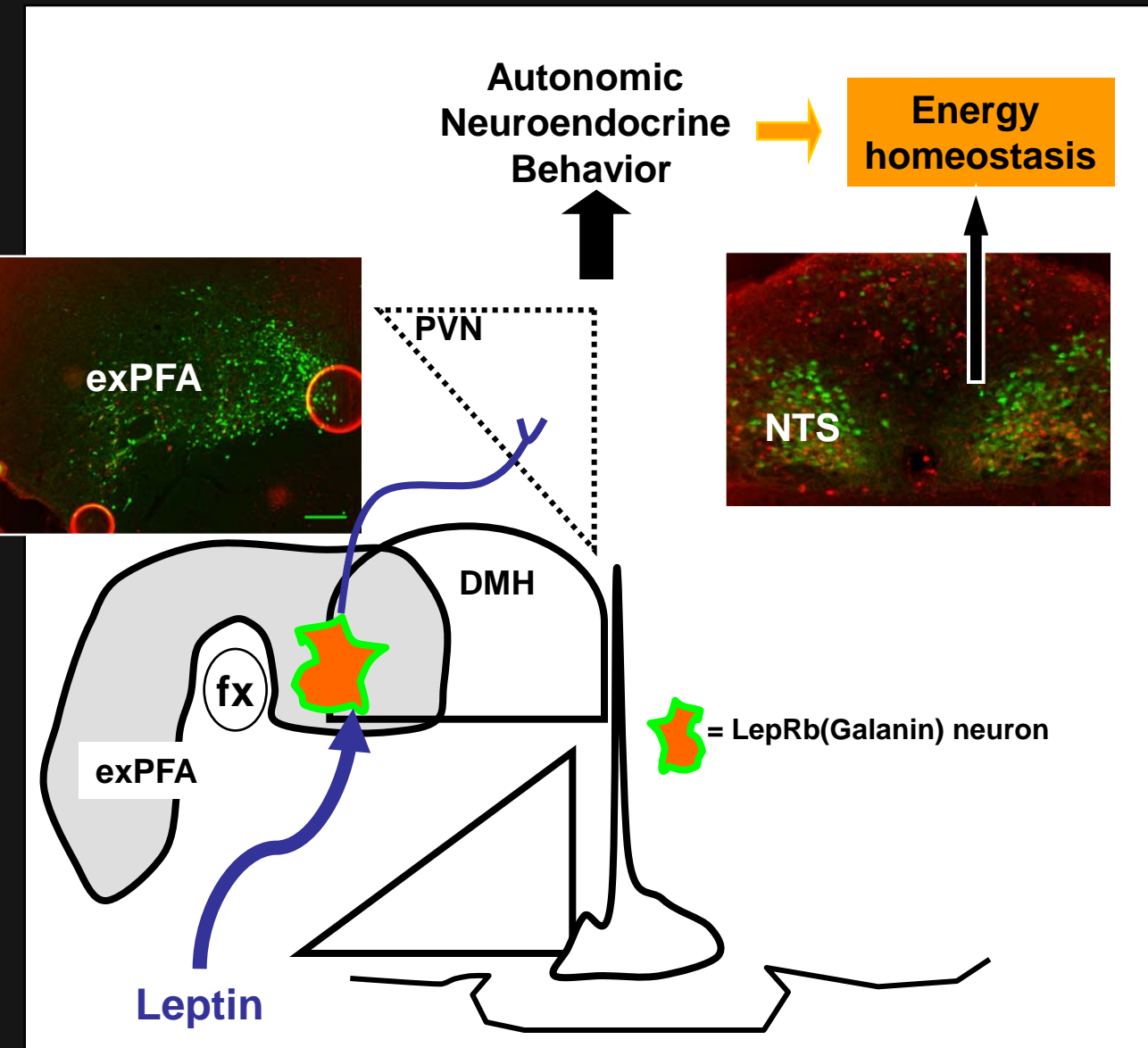


* Ipsilateral injection site

PFA LepRb neurons



Summary



1. LepRb(Gal) neurons describe a confined neuronal population within the exPFA, as well as the NTS.

2. LepRb(Gal) neurons in the exPFA are distinct from well characterized orexin and MCH neurons.

3. LepRb neurons in the exPFA mediate anorexigenic leptin action.

4. LepRb neurons in the vDMH and PFA innervate the PVN and likely regulate neuroendocrine, autonomic and behavioral PVN outputs.

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Mutant Mouse Regional Resource Ctr
(MMRRC)

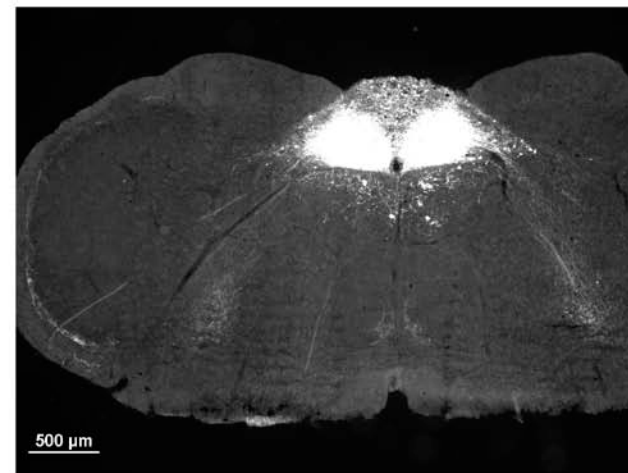
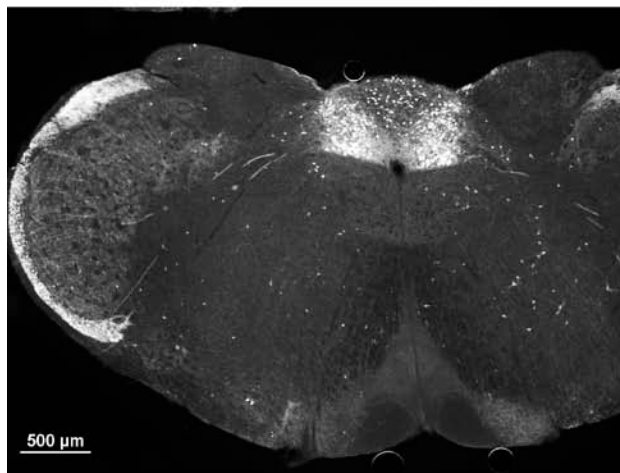
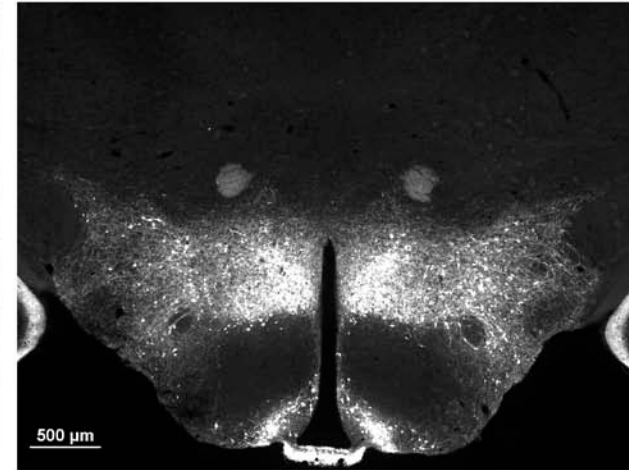
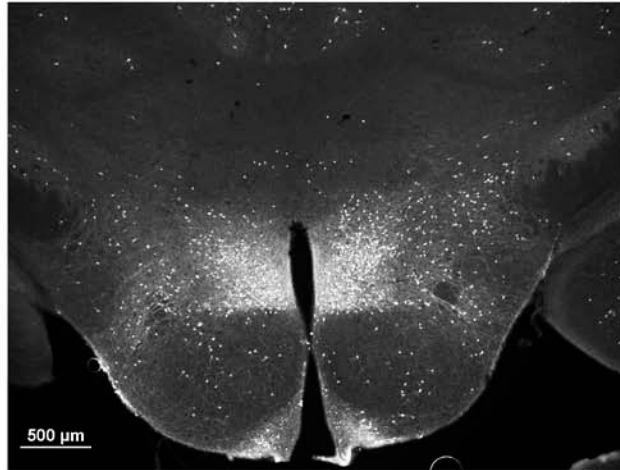
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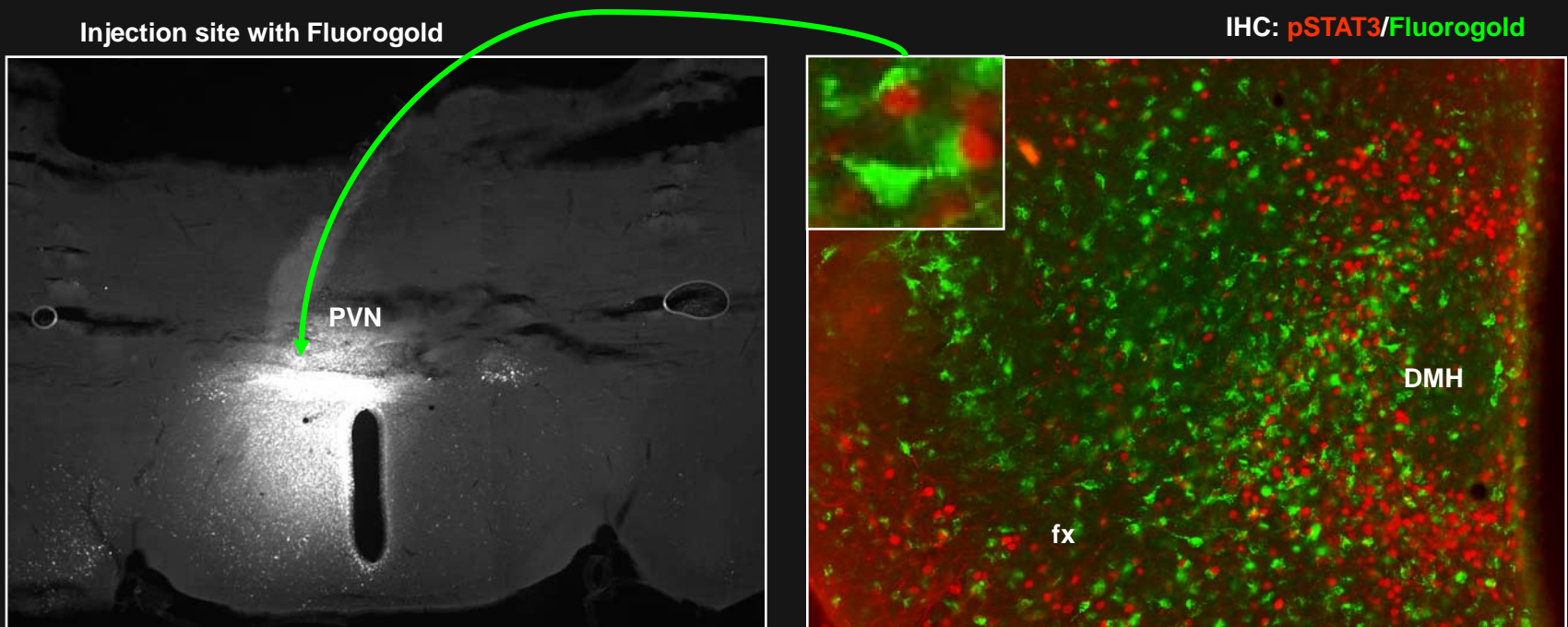
Conditional LepRb deletion in Galanin Neurons: Generation of Galanin^{Cre} Mice

Gal^{Cre/+}, Rosa^{YFP/+}

Gal^{TgGFP}



Classical retrograde tracing experiments: Confirmation of DMH LepRb Projections to the PVN and BST



PVN = paraventricular nucleus
3V = 3rd ventricle
DMH = dorsomedial hypothalamus

Location Might Encode Function and Neuronal Population

